ADHD in the mainstream: the role of emotional dysregulation and overlap with common mental health disorders

Philip Asherson MRCPsych, PhD
Professor of Molecular Psychiatry & Honorary Consultant Psychiatrist,
Social Genetic Developmental Psychiatry, Institute of Psychiatry
Psychology and Neuroscience, King’s College London, UK
ADHD in the mainstream

- Neurodevelopmental disorder
  - early onset
  - late onset

- Neurodiversity

- Mental health disorder (medical treatment)

- Learning Difficulty
Population prevalence rates

Polanczyk et al 2007

5.29%
Prevalence of adult ADHD

Risks of co-occurring disorders

(US national co-morbidity survey)

Rates of ADHD within adult mental health services

Murphy et al., NIHR report, 2013; Deberdt et al., BMC Psychiatry, 2015;
ADHD characterised by two or more symptom domains

Phenotypic correlations ~0.60
Genetic correlations ~0.60
Both dimensions similarly heritable ~0.75
Symptoms of Emotional Impulsiveness in an adult follow-up (mean = age 27) sample of children with ADHD and community controls

Barkley and Fischer, JAACAP, 2010
The unique contribution of Emotional Impulsiveness to psychosocial impairments

Severity of Emotional Instability uniquely contributed to numerous impairments:

• Home life
• Occupation
• Education
• Criminal Activity
• Driving
• Financial outcomes

“EI is as much a component of ADHD as the two traditional dimensions”

Barkley and Fischer, JAACAP, 2010
MIRIAD project
Highly selected sample with no comorbidity and medication free

Recruitment Phase

508 men referred to Maudsley Hospital adult ADHD Clinic between June 2009 and March 2011. All medical records and referral letters screened for study inclusion/exclusion criteria

Most common exclusions

321 individuals excluded
- Other mental health problems: N=162 (e.g. autism: N=45, major depression: N=40; OCD or Tourettes: N=27)
- Current psychoactive medication: N=150
- Substance abuse or addiction: N=96
- Head injury, neurological condition or major cognitive impairment: N=28
More than one of the above in 44% of exclusions.

Screening by telephone

133 individuals excluded
- On medication: N=36
- Not interested: N=32
- Other mental health problems: N=21
- Frequent substance use: N=19
- Unable to contact: N=14

Clinical assessment for ADHD

13 individuals excluded
- Comorbid anxiety disorder and/or OCD: N=4
- Not diagnosed with adult ADHD: N=4
- ADHD in remission: N=3
- Not completing diagnostic assessment: N=2

Final Sample N=41
Sub-threshold psychopathology in ADHD

Skirrow & Asherson 2012
Case-control differences for emotional lability scores

CNS-LS Mean  | ALS-SF Mean  | Anxious-depressed | Depressed-Elated | Anger
---|---|---|---|---
Control | ADHD | Control | ADHD | Control | ADHD | Control | ADHD | Control | ADHD
Average Score (+/- 1 SD)

All p<.001

<table>
<thead>
<tr>
<th>ADHD</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS-Lability scale (CNS-LS)</td>
<td>.88</td>
<td>.83</td>
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<tr>
<td>Affective lability scale (ALS)</td>
<td>.85</td>
<td>.81</td>
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</tbody>
</table>

Skirrow & Asherson JAD, 2013
Predictors of functional impairment in adults with ADHD

<table>
<thead>
<tr>
<th>Impairment/predictors</th>
<th>Beta</th>
<th>R</th>
<th>R²</th>
<th>p</th>
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<tbody>
<tr>
<td><strong>Family</strong></td>
<td></td>
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<tr>
<td>Emotional lability (CNS-LS)</td>
<td>.59</td>
<td>.59</td>
<td>.35</td>
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<td><strong>Education</strong></td>
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<td>.44</td>
<td>.44</td>
<td>.19</td>
<td>.013</td>
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<td><strong>Life Skills</strong></td>
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<td>Emotional lability (CNS-LS)</td>
<td>.61</td>
<td>.61</td>
<td>.38</td>
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<td><strong>Self concept</strong></td>
<td></td>
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<td>Comorbid symptoms (CIS-R)</td>
<td>.55</td>
<td>.55</td>
<td>.30</td>
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<td><strong>Social problems</strong></td>
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<tr>
<td>Emotional lability (CNS-LS)</td>
<td>.35</td>
<td>.56</td>
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<td>&lt;.001</td>
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<tr>
<td>Hyperactivity-impulsivity (BRS)</td>
<td>.35</td>
<td>.68</td>
<td>.40</td>
<td>&lt;.001</td>
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<tr>
<td><strong>Risk (inverse transformed)</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Hyperactivity-impulsivity (BRS)</td>
<td>-.48</td>
<td>.48</td>
<td>.23</td>
<td>.001</td>
</tr>
</tbody>
</table>

Skirrow & Asherson, JAD, 2013
The Experience sampling method (ESM)

- Participant wears a watch which vibrates at varying intervals
- Then they fill out a questionnaire on the PDA
- Responses collected 8 times a day for a working week (mon-fri)
Anger ratings for individuals with ADHD and healthy controls over the 5-day period

Adapted from Skirrow et al., Pschol Med, 2014; KCL PhD 2013
Experience sampling of emotional symptoms

Reported anger +/- 1SE

Average duration from reporting of bad event (mins)

Skirrow et al., Pschol Med, 2014
Affective instability in borderline personality (BPD) disorder, post-traumatic stress disorder (PTSD), bulimia nervosa (BN) and healthy controls (HC): a trans-diagnostic construct

Ratings every 15 minutes during 24 hours.

Santangelo et al., J Abnorm Psychol, 2014, 123: 258-272
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Santangelo et al., J Abnorm Psychol, 2014, 123: 258-272
# Wender-Reimherr Adult ADHD Diagnostic Scale (WRAADS)

## Emotional Dysregulation Items

<table>
<thead>
<tr>
<th>Affective lability</th>
<th>Temper control</th>
<th>Emotional over-reactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mood fluctuations</td>
<td>Irritability</td>
<td>Overwhelmed</td>
</tr>
<tr>
<td>Dysphoric periods</td>
<td>Temper outbursts</td>
<td>Emotional reactivity</td>
</tr>
<tr>
<td>Boredom</td>
<td>Lack of control</td>
<td>Impairment</td>
</tr>
<tr>
<td>Overstimulation</td>
<td></td>
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</tbody>
</table>
ADHD symptoms

Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>ES (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adler et al. 2013 (LDX)</td>
<td>-0.45 (-0.76, -0.13)</td>
</tr>
<tr>
<td>Reimherr et al. 2007 (MPH)</td>
<td>-0.83 (-1.48, -0.18)</td>
</tr>
<tr>
<td>Reimherr et al. 2005 (ATX)</td>
<td>-0.53 (-0.72, -0.34)</td>
</tr>
<tr>
<td>Adler et al. 2014 (ATX)</td>
<td>-0.56 (-0.77, -0.36)</td>
</tr>
<tr>
<td>Goto et al. 2011 (ATX)</td>
<td>-0.62 (-0.82, -0.41)</td>
</tr>
<tr>
<td>Wender et al. 2011 (MPH)</td>
<td>-2.25 (-2.71, -1.78)</td>
</tr>
<tr>
<td>Marchant et al. 2011 (MPH)</td>
<td>-1.10 (-1.65, -0.55)</td>
</tr>
<tr>
<td>Retz et al. 2012 (MPH)</td>
<td>-1.04 (-1.37, -0.71)</td>
</tr>
<tr>
<td>Rosler et al. 2010 (MPH)</td>
<td>-0.31 (-0.47, -0.16)</td>
</tr>
<tr>
<td>Overall (I-squared = 88.9%, p = 0.000)</td>
<td>-0.80 (-1.07, -0.53)</td>
</tr>
</tbody>
</table>
Subgroup analyses

<table>
<thead>
<tr>
<th>Sub-analyses domain</th>
<th>Studies</th>
<th>SMD&lt;sup&gt;a&lt;/sup&gt;</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulants on ED</td>
<td>1,2,6-9</td>
<td>-0.57</td>
<td>-0.80 to -0.34</td>
</tr>
<tr>
<td>Atomoxetine on ED</td>
<td>3-5</td>
<td>-0.21</td>
<td>-0.34 to -0.08</td>
</tr>
<tr>
<td>Stimulants + WRAADDSS-EDS</td>
<td>2,6-9</td>
<td>-0.64</td>
<td>-0.91 to -0.36</td>
</tr>
<tr>
<td>Atomoxetine + WRAADDSS-EDS</td>
<td>3</td>
<td>-0.32</td>
<td>-0.50 to -0.13</td>
</tr>
<tr>
<td>Stimulants + BRIEF-A</td>
<td>1</td>
<td>-0.38</td>
<td>-0.68 to -0.04</td>
</tr>
<tr>
<td>Atomoxetine + BRIEF-A</td>
<td>4,5</td>
<td>-0.15</td>
<td>-0.30 to 0.00</td>
</tr>
</tbody>
</table>

<sup>a</sup> Negative SMD favours a treatment effect for the active medication (stimulants or Atomoxetine)

1= Adler et al., 2013; 2= Reimherr et al., 2007; 3= Reimherr et al., 2005; 4= Adler et al., 2014; 5= Goto et al., 2011; 6= Wender et al., 2011; 7= Marchant et al., 2011; 8= Retz et al., 2012; 9= Rösler et al., 2010
Treatment algorithm

Chronic mental health problem (inattention, hyperactivity, impulsivity, emotional dysregulation)

Screen for ADHD

No ADHD

Establish alternative diagnosis and treat accordingly (e.g. Bipolar disorder, personality disorder/ODD, anxiety/depression, alcohol/drug abuse, severe mood dysregulation)

Yes ADHD

No comorbidity or comorbid personality disorder

** Drug treatment for ADHD (stimulants or atomoxetine)

** In children consider non-drug intervention first, if mild to moderate impairment

Significant depression, bipolar disorder, other condition

Treat comorbid disorder first in most cases

Review and consider additional treatments: CBT, anger management, other medication
Common symptoms seen in adult ADHD

- Emotional instability: irritability, anger, affective lability
- Sleep onset (initial) insomnia
- Feeling restless (agitated when severe)
- Talking excessively or tangentially (severe ADHD)
- Low self-esteem
- Concentration difficulties
- Distractibility
- Impulsivity
- Mind wandering and ceaseless mental activity

ADHD and co-occurring mental health problems

A. Symptoms of ADHD (mimicking other disorders)

B. Overlapping neurodevelopmental disorders, specific and general learning difficulties

C. Development of co-occurring mental health disorders

Asherson et al., Lancet Psychiatry, 2016, 3: 568-78
Symptoms and impairments of ADHD that can mimic other disorders

- **Anxiety:** excessive mind wandering, worrying about performance deficits, feeling overwhelmed, feeling restless, avoidance of situations due to ADHD symptoms (e.g. waiting in queues, social situations requiring focused attention), and sleep problems linked to mental restlessness

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- **Depression:** chronic low self-esteem, unstable moods, impatience, irritability, poor concentration, sleep disturbance

- **Personality disorder (e.g. borderline):** chronic trait-like psychopathology, behavioural problems, emotional instability, impulsive behaviour, poor social relationships

- **Bipolar disorder:** Restlessness and overactivity, sleep disturbance, mood instability, ceaseless unfocused mental activity, distractibility

Asherson et al., Lancet Psychiatry, 2016, 3: 568-78
Increasing the specificity of ADHD symptoms

Attention Dysregulation Hyperactivity Disorder

ADHD symptoms are not core deficits

- Cluster of symptoms
- Hyper-focus
- Sensitivity to salience/reward
- Bored quickly and lose focus
- Spontaneous unconstrained mind wandering
- Impatience when waiting
- Happier when on the go doing something – irritable when there is nothing to do
A meta-analysis of the prevalence of attention deficit hyperactivity disorder in incarcerated populations

S. Young\textsuperscript{1,2*}, D. Moss\textsuperscript{3}, O. Sedgwick\textsuperscript{4}, M. Fridman\textsuperscript{5} and P. Hodgkins\textsuperscript{6}

Estimated prevalence = 25.5%
Impact of adult ADHD on criminality

Proportion of Swedish adults with criminal convictions over a 4-year period (Jan 1, 2006 to Dec 31, 2009)

- Men: 36.6% (ADHD) vs 8.9% (General population)
- Women: 15.4% (ADHD) vs 2.2% (General population)

Medication for ADHD and criminality: observational Swedish database analysis

Hazard ratio for conviction for any crime during ADHD medication (2006–2009) vs. non-medication periods

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Men (n = 16,087) Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All medications</td>
<td>0.68 (0.63–0.73)</td>
</tr>
<tr>
<td>Stimulants</td>
<td>0.66 (0.61–0.71)</td>
</tr>
<tr>
<td>Atomoxetine</td>
<td>0.76 (0.63–0.91)</td>
</tr>
<tr>
<td>SSRI medication</td>
<td>1.04 (0.93–1.17)</td>
</tr>
</tbody>
</table>

- Crimes occurred less often during medication periods:
  - men 32% reduction
  - women 41% reduction

Association Between Prescription of Major Psychotropic Medications and Violent Reoffending After Prison Release

Zheng Chang, PhD; Paul Lichtenstein, PhD; Niklas Långström, MD; Henrik Larsson, PhD; Seena Fazel, MD

Figure 1. Between-Individual Associations Between Psychotropic Medications and Violent Reoffending Following Prison Release

<table>
<thead>
<tr>
<th>Medication</th>
<th>Medicated Periods</th>
<th>Nonmedicated Periods</th>
<th>Risk Difference in No. of Violent Reoffenses/1000 Person-Years (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Individuals, No.</td>
<td>Person-Years</td>
<td>Individuals, No.</td>
<td>Person-Years</td>
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<td>Antipsychotics</td>
<td>2063</td>
<td>1590</td>
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<tr>
<td>Antidepressants</td>
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<td>3831</td>
<td>224</td>
<td>7297</td>
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<td>Psychostimulants</td>
<td>1197</td>
<td>1647</td>
<td>94</td>
<td>1343</td>
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<tr>
<td>Drugs used in addictive disorders</td>
<td>2063</td>
<td>1164</td>
<td>46</td>
<td>3009</td>
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<tr>
<td>Antiepileptics</td>
<td>2213</td>
<td>1972</td>
<td>152</td>
<td>2703</td>
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<tr>
<td>Adrenergic inhalants&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2370</td>
<td>1289</td>
<td>38</td>
<td>2844</td>
</tr>
</tbody>
</table>

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<sup>a</sup> Includes amphetamines and other stimulants.
Association Between Prescription of Major Psychotropic Medications and Violent Reoffending After Prison Release

Zheng Chang, PhD; Paul Lichtenstein, PhD; Niklas Långström, MD; Henrik Larsson, PhD; Seena Fazel, MD

Figure 2. Within-Individual Associations Between Psychotropic Medications and Violent Reoffending Following Prison Release

<table>
<thead>
<tr>
<th>Medication</th>
<th>Medicated Periods</th>
<th>Nonmedicated Periods</th>
<th>Risk Difference in No. of Violent Reoffenses/1000 Person-Years (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
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<tbody>
<tr>
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<td>Individuals, No.</td>
<td>Person-Years</td>
<td>Violent Reoffenses, No.</td>
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<td>1596</td>
<td>100</td>
<td>-39.7 (-57.7 to -11.3)</td>
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<td>Antidepressants</td>
<td>5660</td>
<td>3846</td>
<td>224</td>
<td>5.9 (-11.1 to 28.1)</td>
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<td>Psychostimulants</td>
<td>1202</td>
<td>1648</td>
<td>94</td>
<td>-42.8 (-67.6 to -2.2)</td>
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<tr>
<td>Drugs used in addictive disorders</td>
<td>2077</td>
<td>1168</td>
<td>46</td>
<td>-36.4 (-54.0 to -2.1)</td>
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<td>Antiepileptics</td>
<td>2235</td>
<td>1976</td>
<td>152</td>
<td>10.4 (-15.6 to 48.3)</td>
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<td>Adrenergic inhalants³</td>
<td>2387</td>
<td>1291</td>
<td>38</td>
<td>-7.6 (-17.1 to 55.4)</td>
</tr>
</tbody>
</table>
The CIAO Project

Professor Philip Asherson- Chief Investigator

Clare Evans- Research Worker/Project Coordinator

Co-investigators: Susan Young, Andrew Forester, Declan Murphy

MRC Social Genetic and Developmental Psychiatry

South London and Maudsley NHS Foundation Trust

HM Prison Service
CIAO: A pilot study of Concerta XL In Adult Offenders with ADHD

Aim: To evaluate the effectiveness of Concerta XL in reducing levels of aggression, increasing engagement with educational activities and reducing symptoms of ADHD, in young male offenders with ADHD

Method: 12-week open label study of 100 offenders with ADHD, with 6-month extension.

Drug: Concerta XL 18 – 90 mg titrated to optimal effect

Participants: Male prisoners aged 18-30 (most 18-24)

Site: The trial will take place at HMPYOI Isis.
The CIAO study

- Screened
  - N = 1,922

- Screen positive
  - N = 473 (25%)

- Diagnostic assessment
  - 398 (84%)

- Positive assessments
  - N = 278 (77%)

- 19.3% of prison population met DSM-5 ADHD criteria
- 121 (40%) treated with OROS-MPH

CIAO: final report 2015
Abuse potential and diversion

- Stimulants are controlled drugs with risk for diversion – but diversion in the community usually by college students
- Psychiatric drugs diverted within prisons (e.g. Mirtazapine, Quetiapine)
- Limited abuse potential unless insufflated or injected
- Preparations that are difficult to abuse: Concerta XL and Elvanse

Limited drug seeking behaviour observed in Concerta trial

<table>
<thead>
<tr>
<th>% titrated to each dose</th>
<th>18 mg</th>
<th>36 mg</th>
<th>54 mg</th>
<th>72 mg</th>
<th>90 mg</th>
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<tbody>
<tr>
<td></td>
<td>0.21</td>
<td>0.34</td>
<td>0.20</td>
<td>0.20</td>
<td>0.04</td>
</tr>
</tbody>
</table>
CIAO: Observer rated ADHD symptoms scores

CIAO: final report 2015
Investigator rated emotional instability
Temper control; Mood lability (AL); Emotional Reactivity (ER)

P<.0001 for all baseline to week 5 changes

CIAO: final report 2015
CIAO: Maudsley Violence Questionnaire

Baseline vs 12-week comparison:
- MVQ-A: NS
- MVQ-M: P<.005
Preliminary report: Number of critical incidents recorded in prison records:

- Total critical incidents includes:
  - Total serious assault
  - Total assault
  - Total fights
  - Total property damage
  - Total self harm
  - Total taking drugs
  - Total disobey

**CIAO**: Based on data 8\(^{th}\) December 2013
# Summary of significant effect sizes (Cohen’s d)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cohen’s d ITT</th>
<th>Cohen’s d pp</th>
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</thead>
<tbody>
<tr>
<td><strong>Investigator rated (I) or self-rated scales (S)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inattention (I)</td>
<td>2.27</td>
<td>3.00</td>
</tr>
<tr>
<td>Hyperactivity-impulsivity (I)</td>
<td>2.11</td>
<td>2.78</td>
</tr>
<tr>
<td>Emotional dysregulation (I)</td>
<td>1.49</td>
<td>1.71</td>
</tr>
<tr>
<td>Affective lability (S)</td>
<td>1.19</td>
<td>1.65</td>
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<tr>
<td>MVQ-Machismo (MVQ) (S)</td>
<td>0.60</td>
<td>0.98</td>
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<tr>
<td>MVQ-Acceptance of violence (S)</td>
<td>0.37</td>
<td>0.40</td>
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<tr>
<td><strong>Prison records of behaviour</strong></td>
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<td></td>
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<tr>
<td>Sum of adjudications</td>
<td>0.30</td>
<td>0.53</td>
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<tr>
<td>Percentage attended activities</td>
<td>0.07 (ns)</td>
<td>0.34</td>
</tr>
<tr>
<td>Sum of positive IEPs</td>
<td>0.25</td>
<td>0.36</td>
</tr>
<tr>
<td>Days in enhanced regime</td>
<td>0.14</td>
<td>0.19</td>
</tr>
</tbody>
</table>

CIAO: final report 2015
ADHD

Education and occupation

Impulsivity and emotional dysregulation
Feedback from Prison Inspectorate

- Outside unbiased perspective
- Inspectors highlighted the CIAO project:

  “All prisoners were offered screening for attention deficit hyperactivity disorder (ADHD) through the specialist Concerta (an ADHD treatment) in adult offenders (CIAO) trial…Some prisoners on the CIAO programme to whom we spoke were experiencing some stability of behaviour for the first time in their lives.”

The HMIP report recommended continued support beyond the prison:

  “There should be efforts to ensure the continued prescribing of medication and ongoing specialist support for prisoners started on the CIAO trial following their release”

Her Majesty’s Inspectorate of Prisons’ report carried out in February of 2014
Thanks!

**Collaborators**
- Jonna Kuntsi
- Caroline Skirrow
- Andrew Merwood
- Celeste Cheung
- Celine Ryckaert
- Ruth Cooper
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